

Bacillary angiomatosis triggered by severe trauma in a healthy Caucasian patient: A case report

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Abstract. Bacillary angiomatosis represents a cutaneous and systemic infection caused by *Bartonella* species, typically described in the past in HIV-positive patients or associated with immunodeficiencies. More recent case reports had brought into attention the probability that this entity may manifest in otherwise healthy individuals, triggered by trauma and skin burns. The physiopathology of this neoproliferative process is based on the production of angiogenetic molecules, such as vascular endothelial growth factor (VEGF) and IL-8. In case of an inadequate treatment, the evolution can be fatal, with a systemic dissemination of the abscesses within the gastro-intestinal tract, respiratory tract, brain and bones. The appropriate therapy is with oral erythromycin and doxycycline, but several treatments such as cephalosporins, penicillins, macrolides, aminoglycosides, rifampin, dapsone, ciprofloxacin, have been tried with favorable results. Herein we present the case of a Caucasian patient, seronegative for HIV, who developed multiple vascular papules and nodules on the face, after a severe trauma and which healed after an adequate antibiotic therapy with oral clarithromycin.

Introduction

Bacillary angiomatosis is an angioproliferative cutaneous and extracutaneous disease, caused by infection with the intracellular Gram-negative coccobacillus *Bartonella* species (*Bartonella* (B) *henselae* and *Bartonella* (B) *quintana*) (1). The physiopathology of this neoproliferative process is based on the production of angiogenetic molecules, such as vascular endothelial growth factor (VEGF) and IL-8 (1-3).

Cats are the most important reservoir for *B. henselae* and the transmission between cats is realised through a flea vector (*Ctenocephalides felis*) (4). In immunocompetent patients, the infection with this bacterium can lead to the 'cat scratch disease' (5). In these situations, almost 90% of patients admit a recent contact with a cat (a scratch or a bite) (4). In both immunodeficient and immunocompetent patients, *B. henselae* can produce bacillary angiomatosis, but in this case, fleas may play a major role in transmitting the infection to humans, considering the fact that only 20% of patients or less admit exposure to cats (4,6). In order to sustain this hypothesis, *B. henselae* DNA was detected in fleas (7-9).

B. quintana has a human reservoir and among humans it can be transmitted by body lice (*Pediculus humanus*) and fleas as well, especially in the context of poverty, lack of hygienic conditions and homelessness (5,10). Moreover, it was the causative organism of trench fever among militaries in World War I (11).

Case report

We present the case of a 43-year-old patient, who had an impressive facial eruption evolving for three weeks, associated with cervical lymphadenopathy. Consent for publication was obtained from the patient. Clinical examination revealed multiple angiomatous erythematous papules and nodules on

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Figure 1. The aspect of the eruption before treatment: angiomatous papules and nodules covered by hematic and honey-like yellowish crusts.



Figure 2. The aspect of the eruption one month after treatment: two remnant papules on the face.

the nasal pyramid, philtrum region, right supraorbital area, mental protuberance and right commissure of the lips, either isolated or grouped, some of them covered by hematic and honey-like yellowish crusts (Fig. 1).

The lesions appeared one week after a severe local trauma produced by a bicycle accident. In the place where the wound on the nose was sutured, the patient noticed red macules that evolved very quickly into papules and nodules, followed by the appearance of other lesions on the face. The oral cavity was normal and he did not have any other complains. He denied any contact with cats or travel in other countries. The clinical aspect of the eruption pointed towards the diagnosis of bacillary angiomatosis.

Results

The complete blood count, blood chemistry, liver and renal tests, urine analysis and erythrocyte sedimentation rate were within normal values and pulmonary radiography and abdominal ultrasound did not show any anomalies. HIV serology assessed by ELISA was negative, as well as the screening tests for hepatitis B and C. A bacterial culture performed from the lesion showed *Staphylococcus aureus* colonization.

Histopathological examination revealed in the dermis a diffuse proliferation of small caliber vascular structures, some of them dilated, lined by edematous endothelial cells. The edematous stroma was associated with a

polymorphous inflammatory infiltrate (mostly neutrophils, but also lymphocytes, plasma cells and histiocytes) dispersed throughout the lesion. Moreover, derma-epidermal ulceration was present, with a necrotic detritus with fibrin, leucocytes and small microbial colonies, and positive Giemsa and Warthin Starry stains. The histopathological findings were compatible with pyogenic granuloma/bacillary angiomatosis or *verruca peruana*. *Verruca peruana* was excluded because the patient denied traveling in South America. *In vivo* imaging techniques do not provide much support for the diagnosis, although progress has been made in recent years in some inflammatory skin diseases (12).

The patient was prescribed clarithromycin 500 mg twice daily for six weeks. After the first ten days of treatment, a gradual reduction in size of the lesions was observed. After one month, there were only two remnant papules on the face that were shave biopsied (Fig. 2). Considering the clinical aspect of the lesions, the histopathological findings and the rapid remission after initiation of the antibiotic treatment (which is not characteristic for pyogenic granuloma) a final diagnosis of bacillary angiomatosis was made. In the year of follow-up, there was no recurrence.

Discussion

Bacillary angiomatosis was first described several decades before in HIV-positive patients (13) as an opportunistic infection, but it may also occur in the context of other conditions that

may impair the immune status, such as chronic lymphocytic leukemia (11,14,15), chemotherapy (16), systemic corticotherapy (17), solid organ transplantation (18-20), hepatitis B infection (3). Nevertheless, immunocompetent patients can be affected by this cutaneous disorder (6,17,21-24). It can also appear in pediatric patients (20,24,25).

The presented patient was HIV, HBV (hepatitis B virus) and HCV (hepatitis C virus) negative, other causes of immunosuppression were absent and he was not taking any drugs.

Only a case with lesions on the face resembling those of the presented patient was found in the literature, that appeared on the site of a recent burn (6), as well as lesions induced by recent trauma (3). Moreover, a healthy child, without any sign of immunodeficiency, developed bacillary angiomatosis on the face after a traumatic wound, as in the case of the presented patient (24). In these cases, the infection could be transmitted by sandflies, ticks or unknown vehicle (3).

Clinically, the lesions may mimic the aspect of pyogenic granulomas, Kaposi's sarcoma or *verruca peruana*, described as bright red, purple or violaceous vascular papules and nodules, with sharp demarcation and a chronic evolution over days to months (7,26,27). The surface may be friable, with tendency to bleed or it may be covered by serous and hematic crust (7). More rarely, the clinical picture may be represented by subcutaneous nodules or indurated plaques (26-29). In HIV patients bacillary angiomatosis presents as a large, subcutaneous tumoral mass (5,30). A case of bacillary angiomatosis in an immunocompetent patient, presenting erythematous nodules on the legs which became ulcerated, has been described (27). The eruption usually involves the face, the neck, the trunk and the limbs, but other regions can be affected as well, including the scalp (22). Bacillary angiomatosis can also affect the mucous membranes (tarsal and oral mucosa) (31).

Clinical examination can reveal one single papule or nodule, but hundreds of lesions can also be present (32). In case of inadequate treatment, the evolution can be fatal, with a systemic dissemination of the abscesses within the gastro-intestinal tract, respiratory tract, brain and bones (5,25,31). Fever, weight loss, anorexia, malaise and lymphadenopathy may be associated complaints (31). In case the abscesses invade the liver or the spleen, *B. henselae* can be the first culprit of this disease called 'bacillary peliosis' (4,19).

The histopathological description correlates with the clinical appearance of the lesions. When pyogenic granuloma-like lesions are seen, microscopy shows elements that are more superficially located, characterized by a lobular proliferation of small vascular structures (capillaries and venules) and plump endothelial cells, associated with an inflammatory infiltrate (with neutrophils, lymphocytes and histiocytes) (18,19,22,26). In other clinical forms, the cellular content is more dense and deeper (22,26). The presence of a dense neutrophilic inflammatory infiltrate and granular amphophilic content may point towards bacillary angiomatosis (22). *Bartonella* spp can not be visualized on conventional hematoxylin-eosin staining, but the granular amphophilic material corresponds with the presence of dark

bacilli on silver dye (7). Moreover, microscopy findings may be similar to those of Kaposi's sarcoma, pyogenic granuloma, angiosarcoma, or insect bite (22). However, in contrast with bacillary angiomatosis, endothelial cells in Kaposi's sarcoma are spindle, flattened and, depending on the stage, form dissecting slit-like vascular spaces, and fascicles with variable erythrocyte extravasation (33). Pyogenic granuloma has a lobular architecture, with neutrophils located at the ulcerated surface of the lesion and without identifiable organisms.

In several case presentations, the final diagnosis was based on the demonstration of clustered or solitary bacilli within or around the vessels on Warthin-Starry silver staining in histopathological fragment of the lesion (6,17,21). Other new diagnosis methods for detection of the bacteria, such as tissue culture, serologic tests and molecular methods (detection of DNA *Bartonella* spp by PCR in the blood or tissue) are available in specialized laboratories (5,31).

Due to financial limitations, in the case of our patient we could not perform DNA detection of *Bartonella* species by PCR and specific serologic tests. Thereby, the final diagnosis was based on the clinical aspect of the lesions, the histopathological report and the rapid remission after initiation of the antibiotic treatment, which excluded other differential diagnosis.

The appropriate therapy is with oral erythromycin (500 mg x4/daily) and doxycycline (100 mg twice daily), but several treatments such as cephalosporins, penicillins, macrolides, aminoglycosides, rifampin, dapsone, ciprofloxacin, have been tried with favorable results (19,31,34,35).

We suggest the importance of further studies regarding treatment strategy in bacillary angiomatosis. There are a small number of published reports, especially in immunocompetent patients. Even if oral erythromycin remains the drug of choice for bacillary angiomatosis, we found some interesting observations: the response to treatment can range from a spectacular and fast one to an incomplete and chronic one; lack of response to erythromycin but adequate response to clarithromycin.

The rapid healing of the eruption in the presented case also suggest the utility of further studies regarding the modulation of endothelial cell proliferation irrespective of the antibacterial potency of the agent used for the treatment. Macrolides interfere with endothelial cells, immune and inflammatory cells. Identifying a drug that optimally combines all these effects may be a goal for other research. Knowing the reported inhibitory effect of clarithromycin on tumor-induced angiogenesis, we also highlight the possible beneficial role of these molecules in the treatment of angioproliferative diseases, with positive or negative infectious etiology.

A consensus regarding the appropriate period of time that the treatment should be prescribed is missing, thereby even though the lesions can disappear within a few days or one-two months, continuing the therapy for three to six months in order to prevent recurrences is the best approach, especially in HIV patients (7,19,31).

In conclusion, the presented case was unique in that the patient was seronegative for HIV and exhibited extensive lesions on the face, after local trauma that remitted rapidly with antibiotic treatment.

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Availability of data and materials

All patient data are mentioned in the article and are available from the corresponding author on reasonable request.

Authors' contributions

MB, RIN, GB, TAT, AB, DAI and GT had substantial contributions to the conception of the work and the acquisition of data for the work. LN, CGP, SAZ and RTA had substantial contributions to the analysis and interpretation of data for the work. All the authors were involved in writing the manuscript and revised the manuscript critically for important intellectual content, approved the final version to be published and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are resolved.

Ethics approval and consent to participate

Patient consent to participate was obtained before publication.

Patient consent for publication

Patient consent for the images was obtained before publication.

Competing interests

The authors declare that they have no competing interests.

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